

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference R 44662	FOR FURTHER ACTION	See item 4 below
International application No. PCT/AT2004/000390	International filing date (<i>day/month/year</i>) 04 November 2004 (04.11.2004)	Priority date (<i>day/month/year</i>) 04 November 2003 (04.11.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant SZELES, Josef, Constantin		

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|---|---------------------|--|-------------------------------------|------------------|----------------------------|--------------------------|-------------------|-----------------|-------------------------------------|--------------------|---|--------------------------|-------------------|-----------------------------------|-------------------------------------|------------------|--|--------------------------|-------------------|--------------------------------|--------------------------|--------------------|---|--------------------------|---------------------|--|
| <p>1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p>In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.</p> | | | | | | | | | | | | | | | | | | | | | | | | | | |
| <p>3. This report contains indications relating to the following items:</p> <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 15%;"><input checked="" type="checkbox"/></td> <td style="width: 15%;">Box No. I</td> <td style="width: 70%;">Basis of the report</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table> | | | <input checked="" type="checkbox"/> | Box No. I | Basis of the report | <input type="checkbox"/> | Box No. II | Priority | <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | <input type="checkbox"/> | Box No. IV | Lack of unity of invention | <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | <input type="checkbox"/> | Box No. VI | Certain documents cited | <input type="checkbox"/> | Box No. VII | Certain defects in the international application | <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. II | Priority | | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention | | | | | | | | | | | | | | | | | | | | | | | | |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VI | Certain documents cited | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application | | | | | | | | | | | | | | | | | | | | | | | | |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application | | | | | | | | | | | | | | | | | | | | | | | | |
| <p>4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).</p> | | | | | | | | | | | | | | | | | | | | | | | | | | |

Date of issuance of this report 27 July 2006 (27.07.2006)	
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yolaine Cussac e-mail: pt11@wipo.int

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

TRANSLATION
PCT

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

(PCT Rule 43bis.1)

Date of mailing (day/month/year)	See form PCT/ISA/210
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Applicant's or agent's file reference R 44662		FOR FURTHER ACTION See paragraph 2 below	
International application No. PCT/AT2004/000390	International filing date (day/month/year) 04.11.2004	Priority date (day/month/year) 04.11.2003	
International Patent Classification (IPC) or both national classification and IPC A61K31/198, A61P25/00			
Applicant SZELES, Josef, Constantin			

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP	Authorized officer
Facsimile No.	Telephone No.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/AT2004/000390

Box No. I	Basis of this opinion
1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.	
<input type="checkbox"/> This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).	
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:	
a. type of material	
<input type="checkbox"/> a sequence listing	
<input type="checkbox"/> table(s) related to the sequence listing	
b. format of material	
<input type="checkbox"/> in written format	
<input type="checkbox"/> in computer readable form	
c. time of filing/furnishing	
<input type="checkbox"/> contained in the international application as filed.	
<input type="checkbox"/> filed together with the international application in computer readable form.	
<input type="checkbox"/> furnished subsequently to this Authority for the purposes of search.	
3. <input type="checkbox"/> In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.	
4. Additional comments:	

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/AT2004/000390

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application
 claims Nos. 6-24 and 26 (IA)

because:

- the said international application, or the said claims Nos. 6-24 and 26 (IA)
relate to the following subject matter which does not require an international preliminary examination (specify):

Claims 6-24 and 26 relate to subject matter which, in the opinion of this Authority, falls under PCT Rule 67.1(iv). Consequently, no expert opinion has been established in respect of the industrial applicability of the subject matter of said claims (PCT Article 34(4)(a)(i)).

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (specify):

- the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.
 no international search report has been established for said claims Nos. _____
 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- has not been furnished
 does not comply with the standard

the computer readable form

- has not been furnished
 does not comply with the standard

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- See Supplemental Box for further details.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/AT2004/000390

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement																			
<p>1. Statement</p> <table> <tr> <td align="center">Novelty (N)</td> <td>Claims <u>1-26</u></td> <td align="center">YES</td> </tr> <tr> <td></td> <td>Claims _____</td> <td align="center">NO</td> </tr> <tr> <td align="center">Inventive step (IS)</td> <td>Claims _____</td> <td align="center">YES</td> </tr> <tr> <td></td> <td>Claims <u>1-26</u></td> <td align="center">NO</td> </tr> <tr> <td align="center">Industrial applicability (IA)</td> <td>Claims <u>1-5 and 25</u></td> <td align="center">YES</td> </tr> <tr> <td></td> <td>Claims _____</td> <td align="center">NO</td> </tr> </table>		Novelty (N)	Claims <u>1-26</u>	YES		Claims _____	NO	Inventive step (IS)	Claims _____	YES		Claims <u>1-26</u>	NO	Industrial applicability (IA)	Claims <u>1-5 and 25</u>	YES		Claims _____	NO
Novelty (N)	Claims <u>1-26</u>	YES																	
	Claims _____	NO																	
Inventive step (IS)	Claims _____	YES																	
	Claims <u>1-26</u>	NO																	
Industrial applicability (IA)	Claims <u>1-5 and 25</u>	YES																	
	Claims _____	NO																	
<p>2. Citations and explanations:</p> <p>Reference is made to the following documents:</p> <p>D1: EHRENPREIS S: "D-phenylalanine and other enkephalinase inhibitors as pharmacological agents: Implications for some important therapeutic application" ACUPUNCTURE AND ELECTRO-THERAPEUTICS RESEARCH 1982 UNITED KINGDOM, vol. 7, no. 2-3, 1982, pages 157-172, XP009043539</p> <p>D2: EHRENPREIS S: "Pharmacology of enkephalinase inhibitors: Animal and human studies" ACUPUNCTURE AND ELECTRO-THERAPEUTICS RESEARCH 1985 UNITED STATES, vol. 10, no. 3, 1985, pages 203-208, XP009043546 ISSN: 0360-1293</p> <p>D3: CHENG R S S ET AL: "A combined treatment with D-amino acids and electroacupuncture produces a greater analgesia than either treatment alone; naloxone reverses these effects" PAIN 1980 NETHERLANDS, vol. 8, no. 2, 1980, pages 231-236, XP002316290</p> <p>D4: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1991, KALYUZHNYI L V ET AL: "THE EFFECT OF AN ENKEPHALINASE BLOCKER ON ACUPUNCTURE RESULTS IN ACUPUNCTURE-SENSITIVE AND ACUPUNCTURE-RESISTANT RABBITS" XP002316291 Database accession no. PREV199294021147</p> <p>D5: EP-A-0 004 040 (MERCK PATENT GESELLSCHAFT MIT BESCHRANKTER HAFTUNG) 19 September 1979 (1979-09-19)</p> <p>Explicit reference is made to the relevant passages only in cases where they have not been mentioned in the international search report.</p>																			

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/AT2004/000390

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Art. 33(2) The subject matter of claims 1-26 is formally novel and thus satisfies the criteria of PCT Article 33(2).

Combination of the following features, which are mentioned in all independent claims, is not disclosed in the prior art:

- (a) point-stimulation therapy together with
- (b) breakdown of substance inhibiting endogenous opioid neuropeptides, which is
- (c) present or administered in a product intended for intravenous infusion.

Art. 33(3) The present application does not meet the requirements of PCT Article 33(3) because the subject matter of claims 1-26 appears not to be inventive.

D1 represents the closest prior art. D1 discloses the use of D-phenylalanine as enkephalinase inhibitor for enhancing the effect of the analgesia achieved by electroacupuncture. The problem to be solved can accordingly be defined as follows:

finding of an improved medicament for enhancing the effect of a point-stimulation therapy.

The present application proposes to solve the stated problem by using a substance which inhibits the breakdown of endogenous opioid neuropeptides and which is present and administered in a product intended for intravenous infusion.

D2 discloses the use of D-leucine, which is to be categorized as equivalent to the use of D-phenylalanine, for intensifying the analgesic effect of methods for point stimulation (acupuncture).

D3 discloses the efficiency of the combined use of D-phenylalanine and D-leucine for the same purpose. The dosages used correspond to the orders of magnitude proposed in the present application.

D4 emphasizes the analgesic efficiency of the

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/AT2004/000390

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

combination of D-phenylalanine with the point stimulation - which is also used in the present application - at sensitive points on the ears. D5 emphasizes the mechanism of the analgesic effect of D-phenylalanine and D-leucine as inhibition of the breakdown of endogenous opioid neuropeptides.

In the light of the prior art teaching, the following is stated:

In relation to the subject matter of claims 1-26, it is pointed out that no basis for acknowledgement of an inventive step is evident in the present application because no evidence is found that the technical features forming the basis for novelty (intravenous infusion) contribute to solving the stated problem in a way which would not have been predictable by a person skilled in the art, since both the basic use of the said substances for enhancing the effect (in particular the analgesia) of methods for point stimulation and the underlying mechanism of the effect were known.

Art. 33(4) The subject matter of claims 1 to 5 and 25 is regarded as industrially applicable within the meaning of PCT Article 33(4).

The PCT Contracting States do not have uniform criteria for assessing the industrial applicability of claims 6-24 and 26 in their present form. Patentability may also depend on the wording of the claims. The EPO, for example, does not recognize the industrial applicability of claims to the medical use of a compound; it may, however, allow claims to the first medical application of a known compound or to the use of such a compound in the manufacture of a drug for a new medical application.